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10/588,005	08/01/2006	Philippe Perovitch	0603-1003	1374

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EXAMINER	
SASAN, ARADHANA	
ART UNIT	PAPER NUMBER
1615	

NOTIFICATION DATE	DELIVERY MODE
01/22/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DocketingDept@young-thompson.com

Office Action Summary	Application No.	Applicant(s)	
	10/588,005	PEROVITCH ET AL.	
	Examiner	Art Unit	
	ARADHANA SASAN	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 13-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 13-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The remarks and amendments filed on 09/21/09 are acknowledged.

2. Claims 11-12 were cancelled. Claims 1-10 and 13-20 were amended. New claims 21-24 were added.

3. Claims 1-10 and 13-24 are included in the prosecution.

Abstract

4. Applicant's submission of a new Abstract (09/21/09) is acknowledged.

Response to Arguments

Rejection of claims 11 and 12 under 35 USC § 101

5. In light of the cancellation of claims 11 and 12, the rejection under 35 USC § 101 with respect to these claims is rendered moot.

Rejection of claims 9 and 10 under 35 USC § 112, 1st paragraph

6. In light of the amendment of claims 9 and 10 to remove the term "metolose" and recite "hydroxy-propyl-methyl cellulose," the rejection under 35 USC § 112, first paragraph, with respect to these claims is withdrawn.

Rejection of claims 1-3 and 9-13 under 35 USC § 112, 2nd paragraph

7. In light of the amendment of claims 1-3 and 13 to remove the terms "derivative of the aryl-carboxylic family," the rejection under 35 USC § 112, second paragraph, with respect to these claims is withdrawn.

8. In light of the amendment of claims 9 and 10 to remove the trademark/trade name "METOLOSE®," the rejection under 35 USC § 112, second paragraph, with respect to these claims is withdrawn.

9. In light of the cancellation of claims 11 and 12, the rejection under 35 USC § 112, second paragraph with respect to these claims is rendered moot.

Rejection of claims 1-8 and 11-20 under 35 USC § 102(b)

10. In light of the cancellation of claims 11 and 12, the rejection under 35 USC § 102(b) as being anticipated by Finidori with respect to these claims is rendered moot.

11. In light of the amendments of claims 1-8 and 13-20, Applicant's arguments, see page 13, filed 09/21/09, regarding the rejection of these claims under 35 USC § 102(b) as being anticipated by Finidori have been fully considered and are persuasive. Therefore, the rejection has been withdrawn.

New claims 21-24

12. Applicant's amendment introduces new claims 21-24. Since the rejection of these new claims was necessitated by Applicant's amendment, this action is made FINAL.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 1-8 and 13-20 **remain** rejected and new claims 21 and 23-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Pankhania et al. (WO 02/083119 A1).

The claimed invention is a composition to be administered as a tablet or lozenge, comprising a low dosage lipophilic non- steroidal anti-inflammatory (NSAID) or anti-mycotic drug under an amino acid salt form, wherein the composition can be passively diffused into buccal and throat mucous membranes when the composition is totally released, dissolved, coated to the mucous membrane, and then absorbed through mucous.

Pankhania teaches a pharmaceutical composition comprising ibuprofen and includes the lysine salt of ibuprofen (Page 1, lines 3-6 and lines 13-14). The compositions are in a form suitable for oral administration (Page 4, lines 24-25). Suitable ingredients (including diluents, lubricating agents, disintegrating agents, binders and flow agents) for the composition include lactose, sucrose, magnesium stearate, alginic acid, croscarmellose sodium, carboxymethyl cellulose, polyvinylpyrrolidone, gelatin, hydroxypropylmethyl cellulose, and talc (Page 5, lines 21-34). Xanthan gum is disclosed as a release retarding agent (Page 6, lines 9-13). Diluents including sorbitol, xylitol, sucrose, flavorings, taste-masking agents, and aspartame are disclosed (Page 7, lines 10-17). Examples 18-23 disclose ibuprofen lysinate, lactose, croscarmellose sodium (sodium carboxymethylcellulose), magnesium stearate and polyvinylpyrrolidone (Page 21, lines 1-25).

Regarding instant claims 1-8, 13-20, and 23-24 the limitations of a tablet or lozenge are anticipated by the compositions in a form suitable for oral administration including tablets, as taught by Pankhania (Page 4, lines 24-35). The limitation of a low dosage lipophilic NSAID is anticipated by the ibuprofen lysinate taught by Pankhania

(Page 21, lines 1-25 Examples 18-23). The limitation of the passive diffusion into buccal and throat mucous membranes is anticipated by the formulations comprising ibuprofen lysinate, lactose, croscarmellose sodium (sodium carboxymethylcellulose), magnesium stearate and polyvinylpyrrolidone (Page 21, lines 1-25) and by the compositions that effervesce when in contact with water (Page 6, line 32 to Page 7, line 4). An effervescent composition will release the active ingredient and since the composition is administered orally, the active agent will be released in the oral/buccal mucosa and will be absorbed through the oral/buccal mucosa. Pankhania teaches the inclusion of taste masking agents because the release of the NSAID in the oral mucosa needs to be palatable enough for subjects to continue the therapeutic regimen. The limitations of the substrate (carbohydrate), amino acid (lysine), polymer agent (cellulose derivative, gum, alginic acid, gelatin, and povidone) are anticipated by the teaching of a composition for oral administration comprising ibuprofen lysinate, lactose, sucrose, magnesium stearate, alginic acid, croscarmellose sodium, carboxymethyl cellulose, polyvinylpyrrolidone, gelatin, hydroxypropylmethyl cellulose, talc, xanthan gum, sorbitol, xylitol, sucrose, flavorings, taste-masking agents, and aspartame, as disclosed by Pankhania (Page 5, lines 21-34, Page 6, lines 9-13, and Page 7, lines 10-17).

Regarding new claim 21, the limitation of the method for producing a medication for treating buccopharyngeal ailments is anticipated by the controlled release composition where the active is incorporated into a matrix containing a release retarding agent, as taught by Pankhania (Page 5, lines 9-11 and Page 6, lines 9-13).

Therefore, the limitations of claims 1-8 and 13-21 are anticipated by the teachings of Pankhania.

Response to Arguments

15. Applicant's arguments, see Page 17, filed 09/21/09, with respect to the rejection of claims 1-8 and 11-20 under 35 USC § 102(b) as being anticipated by Pankhania et al. (WO 02/083119 A1) have been fully considered but are not persuasive.

Applicant argues that "the Pankhania composition is taken by oral route and then metabolized to allow the active ingredients to reach the brain blood flow [to] be pharmacologically effective. It is strictly the typical systemic application of a drug combination against migraine and nausea using the combination of ibuprofen and prochlorperazine."

This is not persuasive because the composition taught by Pankhania can be retained in the oral cavity and since this composition contains all the structural components of the instant claims, the delivery of the active ingredient across the oral or buccal mucosa (i.e., the passive diffusion of the active ingredient across the buccal mucosa) will necessarily occur.

Applicant argues that Pankhania utilizes from 50 to 800 mg of racemic ibuprofen in each dose and that these are high dosages related to a typical systemic application range. This is not persuasive because the lower end of the range of ibuprofen dosage taught by Pankhania is considered low dosage (i.e., 50 mg of ibuprofen). Claims 1-8, 13-21, and 23-24 do not require a specific dosage of ibuprofen. The low dosage of

ibuprofen disclosed by Pankhania encompasses and anticipates the low dosage recitation of claims 1-8, 13-21, and 23-24.

Applicant argues that "the high dosages of ibuprofen used in the Pankhania composition, even when as little as the lowest 50 mg dosage, would recrystallize in the mouth environment and thus encounter the problems detailed in the comments above. The Pankhania composition would not work in a composition to be passively diffused into buccal and throat mucous membranes as recited in claim 1."

Applicant has not provided any evidence of the recrystallization of ibuprofen in the mouth at 50mg dosage level. Pankhania teaches formulations that will release the active ingredient in the mouth, and the active ingredient will be absorbed through the oral or buccal mucosa. Pankhania also teaches an effervescent composition with taste masking ingredients so that when this composition is administered orally and retained in the mouth, the subject finds it palatable. If a tablet was intended strictly for swallowing, taste masking would not be required. Pankhania teaches the inclusion of taste masking agents because the release of the NSAID in the oral mucosa needs to be palatable enough for subjects to continue the therapeutic regimen.

Therefore, the rejection of 06/19/09 is maintained.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. Claims 9-10 remain rejected and new claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Pankhania et al. (WO 02/083119 A1) in view of Mitra (WO 95/07103).

The teaching of Pankhania is stated above.

Pankhania does not expressly teach 25mg of ibuprofen lysinate.

Mitra teaches a pharmaceutical composition comprising from 5 to 50 mg S(+)-ketoprofen lysinate and a pharmaceutical composition comprising from 50 to 800 mg S(+)-ibuprofen lysinate (Page 13, claims 5-6).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a composition comprising ibuprofen lysinate and the polymers and substrates, as taught by Pankhania, use the dosage of 50 to 800 mg ibuprofen lysinate, as suggested by Mitra, and produce the instant invention.

One of ordinary skill in the art would do this because the range of ibuprofen lysinate dosage is known in the art, as evidenced by the teaching of Mitra. One of ordinary skill in the art would have a reasonable expectation of success in producing a functional pharmaceutical product with a 50 to 800mg dosage of ibuprofen lysinate.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Regarding instant claim 9, the limitation of 25mg of ibuprofen lysinate would have been obvious over the dosage of 50 to 800 mg ibuprofen lysinate, as suggested by Mitra (Page 13, claim 6). The limitation of magnesium stearate, talc, aspartame, "metolose", arome, and sorbitol would have been obvious over the magnesium stearate, talc, aspartame, hydroxypropylmethyl cellulose, flavorings and sorbitol as taught by Pankhania (Page 5, lines 21-34, Page 6, lines 9-13 (Page 7, lines 10-17). The recited dosages of the excipients would have been obvious over examples 18-23 disclosed by Pankhania (Page 21, lines 1-25). These are modifiable parameters that one of ordinary skill in the art can vary (by increasing or decreasing the dosage) during the process of routine experimentation. The recited dosages are obvious variants unless there is evidence of criticality or unexpected results.

Regarding instant claim 10, the limitation of 5mg of ketoprofen lysinate would have been obvious over the dosage of 5 to 50 mg ketoprofen lysinate, as suggested by Mitra (Page 13, claim 5). The limitation of magnesium stearate, talc, aspartame, "metolose", arome, and sorbitol would have been obvious over the magnesium stearate, talc, aspartame, hydroxypropylmethyl cellulose, flavorings and sorbitol as taught by Pankhania (Page 5, lines 21-34, Page 6, lines 9-13 (Page 7, lines 10-17). The recited dosages of the excipients would have been obvious over examples 18-23 disclosed by Pankhania (Page 21, lines 1-25). These are modifiable parameters that one of ordinary skill in the art can vary during the process of routine experimentation. The recited dosages are obvious variants unless there is evidence of criticality or unexpected results.

Regarding instant claim 22, the limitation of a method for treating buccopharyngeal ailments (by local permucosal diffusion comprising administering the tablet according to claim 9 to a subject in need thereof) would have been obvious over the oral administration of the dosage forms taught by both Pankhania and Mitra. When the tablet is retained in the mouth, the release of the active ingredient and the absorption of the active ingredient through the oral or buccal mucosa will necessarily occur.

Response to Arguments

18. Applicant's arguments, see Page 19, filed 09/21/09, with respect to the rejection of claims 9-10 under 35 USC § 103(a) as being unpatentable over Pankhania et al. (WO 02/083119 A1) in view of Mitra (WO 95/07103) have been fully considered but are not persuasive.

Applicant argues that "like Pankhania, Mitra relates to a systemic compound to be administered by an oral route, with general effects on the body and organs … Mitra, however, fails to teach or suggest a strictly topical effect by locally releasing low dosage lipophilic anti-inflammatory or anti-mycotic drugs that are passively diffused into buccal and throat mucous membranes."

This is not persuasive because Mitra clearly teaches tablets and lozenges (Page 6, lines 3-5). One of ordinary skill in the art would know that tablets can be retained in the mouth and lozenges are generally retained in the mouth in order to effect the release and absorption of the active ingredient contained in the lozenge. The combined teachings of the tablet of Pankhania (which contains all the structural components of the

instantly claimed invention) and the low dosage of the anti-inflammatory drug that may be in a lozenge form, as taught by Mitra, render obvious the release and diffusion of the active ingredient into the oral or buccal mucosa.

Therefore, the rejection of 06/19/09is maintained and applied to new claim 22.

Conclusion

19. No claims are allowed.

20. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax, can be reached at 571-272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Aradhana Sasan/
Examiner, Art Unit 1615

/Robert A. Wax/
Supervisory Patent Examiner, Art Unit 1615